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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/601,311	06/20/2003	Eric Adam	SYR-AKT3-5001-C1	5023

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EXAMINER	
NASHED, NASHAAT T	
ART UNIT	**PAPER NUMBER**
1656	

DATE MAILED: 04/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/601,311	ADAM ET AL.	
	Examiner	Art Unit	
	Nashaat T. Nashed, Ph. D.	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *17-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 June 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Applicant's election with traverse of Group I, claims 1-16, in the reply filed on January 31, 2006 is acknowledged. The traversal is on the ground(s) that the invention are not distinct because all the proteins in the three groups comprising the amino acid sequence residues 143-438 of SEQ ID NO: 1, and that SEQ ID NO: 2 encodes the amino acid sequence of residues 136-438. This is not found persuasive because SEQ ID NO: 3 is an independent chemical entity from residues 143-438 of SEQ ID NO: 1 and require different searches in the patent and non-patent literature. It should be noted that SEQ ID NO: 3 is intein derivative AKT3 having 556 amino acid residues. Thus, SEQ ID NO: 3 has substantially different chemical structure from that of residues 143-438 of SEQ ID NO: 1, which makes it independent invention and it would require different search from in the patent and non-patent literature, and therefore the restriction is proper between Groups II and I. Also, the restriction between Groups II and III is proper because the method of Group III does not utilize the protein of SEQ ID NO: 3.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-16 are under consideration in this Office action.

The disclosure is objected to because of the following informalities:

(a) The Figure description of Figure 2 is describing a crystal of AKT3 complex. It should state the composition of the complex such as AKT3 of SEQ ID NO: X-ATP complex. The experimental results of the applicants show no ATP or Mg ions bound to the crystal, see paragraph 125 at page 30. Thus, the crystal was not that of a complex, and the specification has to be amended to reflect that.

(b) The abbreviation MME in paragraphs 12, line 3, at page 3; and 197, line 3 at page 48 is not an art-recognized abbreviation and is not defined in the specification.

Appropriate correction is required.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s). In particular, 37 CFR 1.821, which states:

> (d) Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application.

Thus, each time the phrase AKT3 appears in the specification or in the claims and referring to one of the sequences in the sequence listing, it should be accompanied by a sequence identification number (see for example see Figure description of Figures 2-5, paragraphs 132, and 135, and pages 47 and 48. In addition, applicant describes in the specification a protein consisting of the tetrapeptide Cys-Arg-Ser-Leu fused to the N-

terminal of residues 136-461 of SEQ ID NO: 1. Said sequence should be introduced to the sequence listing as SEQ ID NO: 4.

New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application because: (i) Figure 1 contains 3 parts and should be marked (a), (b) , and (c); and (ii) Figure 5 is too small to read the numbers in the Figures. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Understanding of the Examiner:

The examiner understand from reading the specification, in particular, examples 1 and 2 that the protein used to obtain the crystal of the invention consists of the tetrapeptide Cys-Arg-Ser-Leu fused to the N-terminal of the protein of residues 136-461 of SEQ ID NO: 1 (should be new SEQ ID NO: 4). It further assumed that the stock solution of the protein solution contains 50% egg-white lysozyme. If this understanding is correct, applicant should acknowledge the understanding. Otherwise, applicant should correct the examiner's understanding of the specification with specific references therein.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-15 are directed to all possible crystals of AKT3 protein having 90% and 95% sequence identity to residues 143-438 of SEQ ID NO: 1 from any biological source, and a method of crystallizing said protein. Claims 9-15 are directed to a method of crystallizing the protein using any protein solution comprising any ingredients and using any precipitant at any concentration. The specification, however, only provides a single representative species of these crystals, an orthorhombic crystal in space group $P2_12_12_1$ with unit cell dimensions a = 48.36 Angstrom, b = 72.29 Angstrom, c = 94.52 Angstrom, and $\alpha = \beta = \gamma = 90$ degrees obtained by a micro sitting drop method under the single set of crystallization conditions cited in paragraphs 194 and 197, at pages 47 and 48 of the specification using 15% PEG MME 5000, and clarified by the examiner

understanding stated above. There is no disclosure of any particular relationship between the primary structure of the polypeptide and the crystallization conditions. The primary amino acid sequence of the polypeptide, which produced the crystal disclosed in the specification, is not apparent. The specification does not even teach the crystallization of a protein consisting of residues 143-438. Also, the specification fails to describe additional representative species of these crystals by any identifying structural characteristics or properties other than the cell dimensions and the space group of claims cited in claims 5 and 6, for which no predictability of structure is apparent. In addition, the specification fails to teach any other set of condition, which produced a suitable crystal for structure determination by the X-ray diffraction method. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Claims 1-15 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification does not enable any person skilled in the art to make and use the invention commensurate in scope with these claims. The claims are broader than the enablement provided by the disclosure with regard to all-possible crystals comprising a portion having at least 90% or 95% to residues 143-438 of SEQ ID NO: 1. Factors to be considered in determining whether undue experimentation is required are summarized *In re* Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claimed invention encompasses any crystal or method to obtain any crystal of a protein in which has 90% or 95% sequence homology to residues 143-438 of SEQ ID NO: 1. The specification provides guidance and examples in the form of an assay to crystallize the polypeptide defined the amino acid sequence of SEQ ID NO: 4 described above. While molecular biological techniques and genetic manipulation to make any protein are known in the prior art and the skill of the artisan are well developed, knowledge regarding crystallization of proteins and their complexes is lacking. It is well established in the art that obtaining a protein and its complexes in a crystal form is highly unpredictable. The skilled artesian would be expected to screen large number of crystallization conditions, which may include screening variety of conditions in space, a micro gravity environment. A protein which may crystallize under specific crystallization condition, it mutants may or may not crystallize under the same condition. In many cases, a protein that can't be crystallized, one of its specific mutants or fragments might be crystallizable. Even if a crystal is

obtained, it may or may not be suitable for structure determination by X-ray crystallography. Applicants should note the amount of work and experimentation required to obtain a protein, its mutant or fragment in crystal, which is not obvious over the wild-type protein is enormous. Thus, searching for a crystallization conditions for a protein and its complexes that is suitable for X-ray crystallography is well outside the realm of routine experimentation and predictability in the art of success in is extremely low. The amount of experimentation to identify a crystallization condition of an analog having an amino acid sequence of 90% or 95% homologus to residues 143-438 of SEQ ID NO: 1 from any biological source or its cystallizable mutants and fragments, and identify a crystal suitable for structure determination by X-ray crystallography is enormous. Since routine experimentation in the art does not include screening large number of crystallization conditions or mutants which can be crystallized where the expectation of obtaining the desired crystal is unpredictable, the Examiner finds that one skilled in the art would require additional guidance, such as information regarding the exact amino acid sequence of the AKT3 protein, its variant or fragment thereof, and the crystallization conditions that produce a crystal suitable for structure determination by X-ray crystallography. Without such guidance, the experimentation left to those skilled in the art is undue.

> The following is a quotation of the second paragraph of 35 U.S.C. 112:
> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim 16 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "at least a portion of a protein expressed as a nucleic acid molecule that comprises SEQ ID NO: 2" in claim 16 renders the claim indefinite because the resulting claim does not define the metes and bound of the claimed invention. For examination purposes only, the claim is assumed to be directed to the amino acid sequence of SEQ ID NO: 1 or any fragment there of comprising residues 136-461 of SEQ ID NO: 1.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical

Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claim 16 is rejected under 35 U.S.C. 102(e) as being anticipated by U. S. patent 6,881,555 ('555).

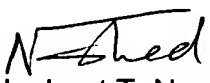
The '555 patent teaches the AKT3 amino acid sequence of SEQ ID NO: 2, see Figures 1 and 1A, and the recombinant expression of ATK3, see starting at column 14, line 38. SEQ ID NO: 2 of the patent comprises residues 136-461 of SEQ ID NO: 1 of the instant application, which is encoded by the nucleic acid sequence of SEQ ID NO: 2.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nashaat T. Nashed, Ph. D. whose telephone number is 571-272-0934. The examiner can normally be reached on MTWTF.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen M. Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Nashaat T. Nashed, Ph. D.
Primary Examiner
Art Unit 1656